OFFICE OF NEW DRUGS

Consulting the Pregnancy and Lactation Team

CONTENTS

PURPOSE

- This MAPP establishes responsibilities and procedures in the Center for Drug Evaluation and Research (CDER) for consulting the Pregnancy and Lactation Team (PLT).
- This MAPP also provides a general description of the PLT's role in pregnancy risk assessment and labeling recommendations.

BACKGROUND

- The PLT is located in the Immediate Office of the Office of New Drugs (OND) and reports to the Deputy Director of OND, who oversees the team's overall priorities and objectives. The PLT is responsible for developing regulations, guidance documents, and procedures related to how drugs are labeled for use during pregnancy and lactation. The PLT also works with, and responds to, consult requests from drug review divisions related to giving advice on postmarketing commitments for pregnancy exposure registries; writing the pregnancy and lactation sections of labeling; developing pregnancy prevention risk management programs; evaluating protocols and analyzing data from industry-sponsored pre- and postmarketing pharmacokinetic, clinical lactation, and safety studies in this area; and evaluating published case reports/case series and epidemiologic studies of possible drug-induced adverse pregnancy outcomes or effects in breast-fed infants.

REFERENCES

- 21 CFR 201.57(f)(6), (7), and (8)
- Guidance for Industry, *Establishing Pregnancy Exposure Registries*
- Guidance for Reviewers, *Evaluating the Risks of Drug Exposure in Human Pregnancies*

- Draft Guidance for Industry, *Pharmacokinetics in Pregnancy — Study Design, Data Analysis, and Impact on Dosing and Labeling*[1]

- Draft Guidance for Industry, *Clinical Lactation Studies — Study Design, Data Analysis, and Recommendations for Labeling*[1]

- Guidance for Industry, *Formal Meetings with Sponsors and Applicants for PDUFA Products*

POLICY

- To ensure consistency across the Center, it is CDER policy for OND review divisions and the Office of Generic Drugs (OGD) to consult the PLT in the following areas:

  – Labeling: when drafting or revising the Pregnancy, Labor & Delivery or Nursing Mothers subsections of product labeling to include human data or change the pregnancy category for all new drug applications (NDAs) or product licensing agreements (PLAs) and for applicable labeling supplements, including CDER-initiated changes.

  – Pregnancy exposure registries: (1) premarketing (when considering the need for a registry and when drafting an approval letter listing a postmarketing agreement for a registry); (2) postmarketing (when evaluating the protocol, reports, or data from a registry).

  – Pregnancy prevention risk management programs: when evaluating the necessity, development, or evaluation of such programs.

  – Other: when evaluating data or epidemiology studies regarding fetal safety following in utero drug exposure.

- Consulting the PLT does not preclude or replace consulting the Office of Drug Safety (ODS) on any drug safety issue involving pregnancy or lactation or the Division of Reproductive and Urologic Products (DRUP) on any issues related to pregnancy or lactation.

- Consults regarding drug efficacy during pregnancy are not within the purview of the PLT and should be referred to DRUP.

[1] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the CDER guidance Web page at http://www.fda.gov/cder/guidance/index.htm.

RESPONSIBILITIES

The Pregnancy and Lactation Team will:

- Provide expertise in assessing risks of drug exposure during human pregnancy and lactation.

- Help the review divisions negotiate with sponsors regarding the need for pregnancy exposure registries as postmarketing study commitments before approval and work with the review divisions to develop language for approval letters regarding the pregnancy exposure registries.

- Review pregnancy exposure registry protocols and make recommendations regarding study design. Review resultant study reports and make recommendations for labeling changes, as appropriate.

- Review proposed pre- or postmarketing pregnancy prevention risk management programs and evaluations of existing programs for highly suspect or known teratogens. Make recommendations regarding program design and strategies.

- Review data from safety studies on human drug exposures during pregnancy and lactation and resultant outcomes. These studies may be ongoing, completed, or published. Make labeling recommendations, as appropriate.

- Review proposed Pregnancy, Labor & Delivery or Nursing Mothers subsections of product labeling for new and marketed drugs, including class labeling and labeling revisions, when based on human data or when the pregnancy category is changed. Recommend labeling changes, as appropriate.

- Review protocols and ensuing study reports for pharmacokinetic studies in pregnant patients, as requested, and make labeling recommendations, as appropriate.

- Review protocols and ensuing study results for clinical lactation studies, as requested, and make labeling recommendations, as appropriate.

- Provide access to special government employees (SGEs) with expertise in human teratology, birth defects, and obstetric pharmacology. Coordinate communications with the SGEs on pregnancy and lactation issues, when appropriate.

- Ensure open communication with DRUP, ODS, and other offices/divisions, if relevant to a particular consult. Consult these groups as needed.

PROCEDURES

CDER Offices and Divisions will:

- Have the consult request form (Form FDA 3291) completed by the review division project manager.

- File all communications in the Division Files System (DFS), attach all supporting documents, and send copies to the PLT Consult Coordinator (pregnancy@cder.fda.gov). Offices that do not use DFS may communicate by other means.

- Contact the PLT for input before issuing an approval letter containing a commitment for a postmarketing pregnancy exposure registry or pregnancy prevention risk management plan.

- Notify the PLT promptly when a consultation involves Prescription Drug User Fee Act (PDUFA) time frames. Provide the desired completion date and justification for the date, including the user fee goal date, pertinent internal or industry meeting dates, and dates for Advisory Committee meetings and meetings with other groups. The PLT generally needs two weeks to prepare for Type A or C industry meetings and four weeks to prepare for Type B meetings.

- Coordinate meeting requests with the PLT as soon as the meeting is requested.

- Consult the PLT for input, as appropriate, when drafting sections of sponsor communications relating to pregnancy and lactation issues.

- Notify the PLT of final actions (including copies of approved labeling) or sponsor communications on any issues on which the PLT was consulted, through DFS or e-mail to pregnancy@cder.fda.gov.

- If DRUP, designate a regulatory project manager as liaison to the PLT.

The PLT Consult Coordinator (Regulatory Project Manager) will:

- Serve as the point of contact for project managers on assignment of reviewers, status of consult requests, and the PLT calendar.

- Enter the appropriate information into and maintain the PLT consult database.

- Ensure that the PLT reviewer enters completed consult reviews into DFS and sends copies to the consult originator and, as appropriate, to ODS (odsconsult@cder.fda.gov) and the DRUP liaison.

- Forward a hard copy of the completed consult review to the originator for those offices that do not use DFS.

The PLT Reviewer will:

- Analyze documents and respond to consultation requests under the supervision of the PLT Team Leader or designated individual.

- Attend meetings as requested by the division or the PLT Team Leader.

- Contact requestors to clarify consultation questions.

- Ask the review division regulatory project manager to consult with ODS, DRUP, or other offices/divisions, when appropriate.

- Obtain information on pregnancy and lactation drug exposures from external sources that include, but are not limited to:

  - *Medline*
  - *Reproductive Hazard Reference (REPROTOX)*
  - Shepard's *Catalog of Teratogenic Agents, Teratogen Information System (TERIS)*
  - Schardein's *Chemically Induced Birth Defects*
  - Briggs's *Drugs in Pregnancy and Lactation*
  - Hale's *Medications and Mothers' Milk*
  - Heinonen's *The Women, Their Offspring, and the Malformations*

- Participate in the review of, and discussions pertaining to, proposed labeling, proposed pregnancy prevention risk management programs, and proposed protocols for pregnancy exposure registries, pharmacokinetic studies in pregnant patients, or clinical lactation studies, as needed.

- Write a detailed response to consults in the standard PLT reviewer template format.

- Obtain concurrence with written consults of the PLT Team Leader and the Deputy Director of OND.

- Enter consultation reviews into DFS and send copies to the consult originators.

- Send copies of consults to ODS (odsconsults@cder.fda.gov), the designated DRUP liaison, or other offices/divisions, as appropriate.

- Provide a hard copy of consults to the PLT Consult Coordinator for forwarding to the consult originator, if not part of DFS.

EFFECTIVE DATE

This MAPP is effective upon date of publication.